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10/530,667

12/19/2005

Ana Martinez Gil

18043-003US1

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FISH & RICHARDSON PC

P.O. BOX 1022

MINNEAPOLIS, MN 55440-1022

EXAMINER

DESAI, RITA J

ART UNIT

PAPER NUMBER

1625

NOTIFICATION DATE

DELIVERY MODE

05/21/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com



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### **DETAILED ACTION**

Claims 1-18 are cancelled.

Claims 19-29 are pending.

Claims 26-29 have been withdrawn.

Claims 19, 20 and 26 have been amended.

The claims have been amended to limit D to be Ch or N and E and G are both either CH<sub>2</sub> or C=O only.

Response to the arguments:-

The rejection under 35 USC 112 has been withdrawn as applicants have amended the claims.

The rejection under 35 USC 103 over WO 01/17529 Hu Ming Kuan et al is also withdrawn as applicants have amended the claims.

The rejection of claims over Fan et al 1997 under 35 USC 103 , has also been withdrawn as applicants have amended the claims.

The rejection of the claims under 35 USC 103 over WO 9102725 Nguyen has been withdrawn as applicants have amended the claimed and argued it convincingly.

The ODP rejection over 10/887,974 still stands as the co-pending application in view of the new art.

The examiner has made new rejection.

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***Claim Rejections - 35 USC § 103***

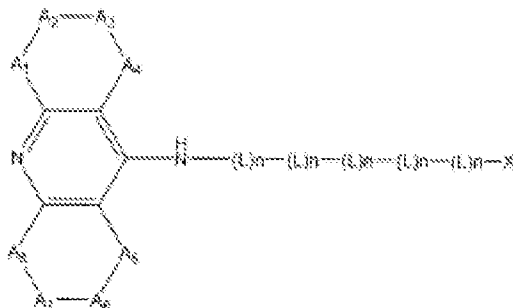
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 19 -25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aranov et al and Caplus Abstract Acheson and Ana Castro Preipheral and Dual Binding site Acetylcholinesterase Inhibitors.

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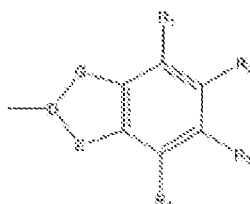
Applicants claims are drawn to compounds of the formula



Formula I

wherein:

X is the following radical:

L is independently selected from  $-C(R)(R')$ ,  $-CO-$ ,  $-O-$  and  $-NR'$ ;

n is zero, one, two, three, four, five, six, seven, eight, nine or ten;

R and R' are independently selected from hydrogen, alkyl, aryl, heteroaryl, halo, haloalkyl, alkoxy, hydroxyl, nitro and alkylthio

D is independently selected from  $-C(R_9)-$ , wherein  $R_9$  is hydrogen, and  $-C-$ , or  $-N-$ A<sub>1</sub>, A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub>, A<sub>5</sub>, A<sub>6</sub>, E and G are independently selected from  $-CO-$ ,  $-C(R_{10})(R_{11})-$ ,  $-C(R_{10})-$ ,  $-N(R_{12})-$ ,  $-N-$ ,  $-O-$ ,  $-S(O)-$ each of E and G is, independently,  $-CO-$  or  $-CH_2-$

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Scope &amp; Content of Prior Art MPEP 2141.01

The Aranov reference teaches the compounds of the formula

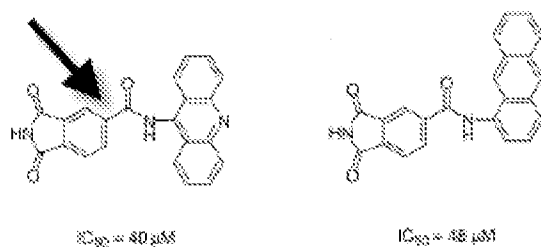
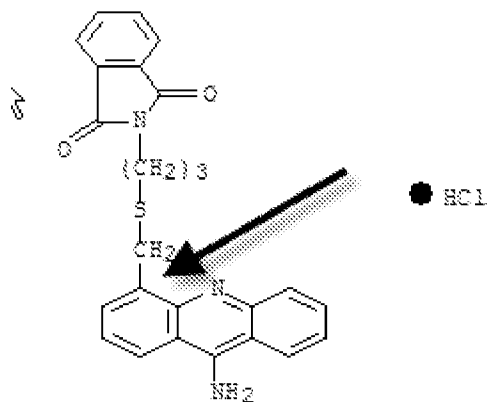


FIG. 1. *G. lamblia* GPR1 inhibitors identified through screening of the in-house chemical database.

The difference is the point of attachment to the indole ring.

Caplus English abstract Acheson et al teaches the compounds



The difference is again the position of attachment.

The Aranov reference attachment of the indole group on the same tricyclic core.

And Acheson teaches the attachment but at a different position on the tacrine. These compounds are very similar in structure and activity to the applicants compounds.

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The teaching of the indole dione core attaches in different ways to the acridine is clearly taught. Even various linkers are taught.

Castro discloses the dual binding ACHE inhibitors. In fig 2 page 260. It teaches the tacrine and the indoyl dione group. Attached via the N. Thus clearly teaching that attaching via the N of the phthaladimide would retain its properties.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

As the attachment of the dione at N position is taught according to Acheson and Castro also teaches the phthalidimide attached via the N to have AChE inhibitor activity., one of skill in the art would be motivated to modify the compounds of Aranov by changing the point of attachment.

Castro further teaches that these are dual binding i.e. both the groups attach to the AChE inhibitor and they teach both the groups the dione indoyl and also the tacrine ( acridine) group, further motivating a person of skill in the art to make compounds with both these groups as a skilled artisan in drug design would realize that they both act as AChE inhibitors.

### ***Conclusion***

Claims 19-25 stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/  
Primary Examiner, Art Unit 1625



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May 17, 2010.